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Claims

(102)

1. A purified retroviral envelope polypeptide, capable of mediating infection of a cell by use of the polytropic/xenotropic receptor encoded by the Rmc1 locus of the NIH Swiss inbred NFS/N mouse for entry, and unable of mediating infection of a cell by use of a human polytropic/xenotropic receptor encoded by the human RMC1 locus.
2. A purified retroviral envelope polypeptide, capable of mediating infection of a cell derived from *Mus musculus* by use of the polytropic/xenotropic receptor encoded by the Rmc1 locus isolated from a NIH Swiss inbred NFS/N mouse for entry, and unable of mediating infection of a human cell solely expressing a human polytropic/xenotropic receptor encoded by the human RMC1 locus.
3. A purified murine retroviral envelope polypeptide, capable of mediating infection of a cell derived from *Mus musculus* using the polytropic/xenotropic receptor encoded by the Rmc1 locus from a NIH Swiss inbred NFS/N mouse for entry, and unable of mediating infection of a human cell comprising a human polytropic/xenotropic receptor encoded by the human RMC1 locus.
4. A purified retroviral envelope polypeptide comprising an amino acid sequence which is at least 94% identical to the amino acid sequence shown in SEQ ID NO: 2, or a fragment of said amino acid sequence that is at least 94% identical to the sequence shown in SEQ ID NO: 2, wherein said polypeptide is capable of mediating infection of a cell by use of the polytropic/xenotropic receptor encoded by the Rmc1 locus of the NIH Swiss inbred NFS/N mouse for entry and unable of mediating infection of a cell by use of a human polytropic/xenotropic receptor encoded by the human RMC1 locus.
5. A purified retroviral envelope polypeptide comprising an amino acid sequence which is at least 94% identical to the amino acid sequence shown in SEQ ID NO: 2, or a fragment of said amino acid sequence that is at least 94% identical to the sequence shown in SEQ ID NO: 2, wherein said polypeptide is capable of mediating infection of a human cell and wherein said polypeptide includes at least one substitution in the VR3 region.

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6. A purified retroviral envelope polypeptide according to claim 5, wherein said mutation is at position 212 in SEQ ID NO: 2.
7. A purified retroviral envelope polypeptide according to claim 5 or 6, wherein said at least one substitution alters the host tropism of a virus or an infectious particle comprising said polypeptide.
8. A purified retroviral envelope polypeptide according to any of claims 5-7, wherein said purified polypeptide is a murine retroviral envelope polypeptide capable of mediating infection of a human cell.
9. A purified retroviral envelope polypeptide according to any of claims 5 to 8, wherein said mutation at position 212 in SEQ ID: 2 results in a methionine.
10. A purified retroviral envelope polypeptide according to any of claims 5-9 capable of mediating a higher infectivity in human cells than MCF-247, MCF-13 and X-MLV (NZB) viruses.
11. A purified retroviral envelope polypeptide according to any of claims 1-10, further comprising an inserted non-viral sequence capable of redirecting the target cell specificity, by the resultant chimeric envelope.
12. A purified retroviral envelope polypeptide according to claim 11, wherein the chimeric envelope further contains secondary mutations, enabling activation of the fusogenic properties of said chimeric envelope, by binding to the receptor target.
13. A purified retroviral envelope polypeptide according to any of claims 11 and 12, wherein said inserted sequence is a single chain antibody.
14. A purified retroviral envelope polypeptide according to any of claims 1-13, further comprising a chemical modification of said envelope.
15. A purified retroviral envelope polypeptide according to claim 14, wherein said chemical modification enhances and/or alters the host tropism.
16. A recombinant mammalian cell displaying an envelope polypeptide according to any of claims 1-15.

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17. An isolated nucleic acid sequence encoding any of the envelope polypeptides according to any of claims 4-15.
18. An isolated nucleic acid sequence as shown in SEQ ID NO: 1
19. A recombinant mammalian expression vector comprising a purified envelope polypeptide according to claims 1-4 and/or 11-15.
- 5 20. A recombinant mammalian expression vector comprising a purified envelope polypeptide according to claims 5-10 and/or 11-15.
21. A replication competent retrovirus, comprising a purified envelope polypeptide according to any of claims 5-10 and/or 11-15.
- 10 22. A replication competent retrovirus comprising an envelope polypeptide according to any of claims 1 to 10 and/or 11 to 15 and further comprising a heterologous translation cassette.
23. A vector according to claim 22, wherein said heterologous translation cassette consists of an IRES-gene element.
- 15 24. A retroviral expression vector comprising a purified envelope polypeptide according to claims 1-4 and/or 11-14.
25. A retroviral expression vector comprising a purified envelope polypeptide according to claims 5-10 and/or 11-15.
- 20 26. A vector according to claim 19 or 20 or 24-25, further comprising at least one heterologous gene to be expressed.
27. A vector according to claim 26, wherein expression of the envelope is directed by a IRES-element.
28. A packaging cell construct comprising a recombinant mammalian expression vector comprising a nucleic acid coding for a purified envelope polypeptide according to any of claims 1-15, and a non-viral or viral promoter and poly-adenylation signals.
- 25 29. Use of a vector according to any of claims 19-20 and/or 28 for the generation of a packaging cell.

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30. Use of a vector according to any of claims 24-27, for expression in a cell constitutively expressing the gag/pol genes of simple retroviruses.
31. Use of a packaging cell according to any of claims 28-30 for the preparation of a composition for the modification of a cell.
- 5 32. Use of a vector according to claims 22 and/or 23, for the preparation of a composition for the modification of a cell.
33. Use of a virus or vector according to any of claims 19-27 or of a replication competent retrovirus comprising a purified envelope polypeptide according to any of claims 1 to 4 and/or 11 to 15 for gene discovery by infection of a new-born rodent.
- 10 34. Use of a virus or vector according to claim 33, wherein said rodent constitutively express the gag/pol genes of simple retroviruses.
35. Use of a virus or vector according to claim 33, wherein said rodent express the gag/pol genes of simple retroviruses in a tissue specific manner.
- 15 36. Use of a virus or vector according to claim 33, wherein said rodent expression of the gag/pol genes of simple retroviruses is developmentally regulated.
37. Use of a virus or vector according to claim 33, wherein said rodent expresses the gag/pol genes of gamma retroviruses tissue specifically and in a developmentally regulated manner.
38. A method for gene discovery comprising
- 20 a) using a virus or vector according to any of claims 19-27 or a replication competent retrovirus comprising an envelope polypeptide according to any of claims 1 to 4 and/or 11 to 15;
- b) infecting a new-born rodent with said virus or vector
- c) inducing a tumour by means of said virus or vector
- 25 d) isolating said tumour in said rodent
- e) identifying a gene involved in the oncogenesis by cloning the integration site of said virus or vector in said tumour.

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39. A method according to claim 38 for gene discovery of a cancer related gene.

40. Use of any of the envelope polypeptides according to claims 1-4 and/or 11-15 or vectors comprising said polypeptides in a bio-safety level 1/PS I/SI laboratory animal facilities or equivalents thereof.

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